Information to Consider for Mirdametinib Coverage (subject to FDA Approval)

Product Overview

Mirdametinib is an investigational, oral, small molecule mitogen-activated protein kinase kinase 1 and 2 (MEK1/2) inhibitor for the potential treatment of adult and pediatric patients 2 years of age and older with neurofibromatosis type 1 (NF1) who have symptomatic plexiform neurofibromas (PNs).[1,2]

Mirdametinib is being investigated in children and adults with neurofibromatosis type 1-associated plexiform neurofibromas (NF1-PN). Mirdametinib has not been approved by the FDA. The safety and efficacy of mirdametinib have not been established. Mirdametinib is currently under review by the FDA with a Prescription Drug User Fee Act (PDUFA) action date of February 28, 2025.

This information is intended for payors, formulary committees, and similar entities to help plan and budget for future coverage and/or reimbursement decisions.

Disease Overview

NF1 is a progressive, neuro-oncology genetic disease that affects multiple organ systems and has a birth incidence of ~1 in 2500.[3,4] Plexiform neurofibromas, a common clinical manifestation of NF1, are highly invasive peripheral nerve sheath tumors that occur in approximately 30%-50% of patients with NF1.[5-7] Patients with NF1-PN may experience debilitating morbidity including severe pain, disfigurement, impaired physical function, internal organ compression, and reduced quality of life.[7,8] Malignant peripheral nerve sheath tumors (MPNSTs) arise from PN, occur in up to 16% of adult patients with NF1, and are associated with a 5-year overall survival rate of up to 50%.[9]

Potential Approval Criteria

Initial Authorization

- Prescribed by or in consultation with an oncologist, neurologist, or other specialists
- The patient is 2 years of age or older; AND
- The patient has BOTH of the following:
    - Diagnosis of neurofibromatosis type 1 (NF1)
    - Symptomatic plexiform neurofibroma (PN)

Duration of initial authorization approval: 12 months.

Potential Reauthorization Criteria

- Prescriber attests that the patient does not show evidence of progressive disease while on therapy and does not experience unacceptable toxicity

Reauthorization will be provided for 12 months.

Potential Drug Class

Antineoplastic: Mitogen-Activated Protein Kinase Kinase (MEK) Inhibitor

Recommended Dosage Forms

- Capsules: 1 mg and 2 mg
- Dispersible tablets (for oral suspension): 1 mg

References: 1. ClinicalTrials.gov. NCT03962543. MEK inhibitor mirdametinib (PD-0325901) in patients with neurofibromatosis type 1 associated plexiform neurofibromatosis (ReNeu). Last updated August 27, 2024. Accessed September 9, 2024. https://clinicaltrials.gov/study/NCT03962543 **2.** Moertel CL, Hirbe AC, Shuhaiber HH, et al; for the ReNeu investigators. ReNeu: a pivotal phase 2b trial of mirdametinib in adults and children with neurofibromatosis type 1 (NF1)-associated symptomatic inoperable plexiform neurofibroma (PN). Presented at: 2024 American Society of Oncology Annual Meeting; May 30-June 3, 2024; Chicago, IL. **3.** Lee T-SJ, Chopra M, Kim RH, Parkin PC, Barnett-Tapia C. Incidence and prevalence of neurofibromatosis type 1 and 2: a systematic review and meta-analysis. *Orphanet J Rare Dis*. 2023;18(1):292. doi:10.1186/s13023-023-02911-2 **4.** New and improved: the way to talk about NF. Children's Tumor Foundation. Press release. Accessed August 12, 2024. https://www.ctf.org/news/new-and-improved-the-way-to-talk-about-nf/ **5.** Ejerskov C, Farholt S, Nielsen FSK, et al. Clinical characteristics and management of children and adults with neurofibromatosis type 1 and plexiform neurofibromas in Denmark: a nationwide study. *Oncol Ther*. 2023;11(1):97-110. doi:10.1007/s40487-022-00213-4 **6.** Prada CE, Rangwala FA, Martin LJ, et al. Pediatric plexiform neurofibromas: impact on morbidity and mortality in neurofibromatosis type 1. *J Pediatr*. 2012;160(3):461-467. doi:10.1016/j.jpeds.2011.08.051 **7.** Miller DT, Freedenberg D, Schorry E, Ullrich NJ, Viskochil D, Korf BR; for the Council on Genetics and American College of Medical Genetics and Genomics. Health supervision for children with neurofibromatosis type 1. *Pediatrics*. 2019;143(5):e20190660. doi:10.1542/peds.2019-0660 **8.** Darrigo LG Jr, Ferraz VEF, Cormedi MCV, et al. Epidemiological profile and clinical characteristics of 491 Brazilian patients with neurofibromatosis type 1. *Brain Behav*. 2022;12(6):e2599. doi:10.1002/brb3.2599 **9.** Higham CS, Dombi E, Rogiers A, et al. The characteristics of 76 atypical neurofibromas as precursors to neurofibromatosis 1 associated malignant peripheral nerve sheath tumors. *Neuro Oncol*. 2018;20(6):818-825. doi:10.1093/neuonc/noy013